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1: Microbiology 2002 May;148(Pt 5):1291-303

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## The ARO4 gene of *Candida albicans* encodes a tyrosine-sensitive DAHP synthase: evolution, functional conservation and phenotypic Aro3p-, Aro4p-deficient mutants.

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The enzyme 3-deoxy-D-arabinoheptulosonate-7-phosphate (DAHP) synthase catalyses the first step in aromatic amino acid biosynthesis in prokaryotes, plant fungi. Cells of *Saccharomyces cerevisiae* contain two catalytically redundant D. synthases, encoded by the genes ARO3 and ARO4, whose activities are feedback-inhibited by phenylalanine and tyrosine, respectively. ARO3/4 gene transcription is controlled by GCN4. The authors previously cloned an ARO3 g orthologue from *Candida albicans* and found that: (1) it can complement an aro3 double mutation in *S. cerevisiae*, an effect inhibited by excess phenylalanine, a homozygous aro3-deletion mutant of *C. albicans* is phenotypically Aro(+), suggesting the existence of another isozyme(s). They now report the identification and functional characterization of the *C. albicans* orthologue of *S. cerevisiae* Aro4p. The two enzymes share 68% amino acid identity. Phylogenetic analysis places the fungal DAHP synthases in a cluster separate from prokaryotic orthologues and suggest that ARO3 and ARO4 arose from a single gene via a gene duplication event early in fungal evolution. *C. albicans* ARO4 mRNA is elevated upon amino acid starvation consistent with the presence of three putative Gcn4p-responsive elements (GCR) in the gene promoter sequence. *C. albicans* ARO4 complements an aro3 aro4 double mutation in *S. cerevisiae*, an effect inhibited by excess tyrosine. The authors engineered Deltaaro3/Deltaaro3 Deltaaro4/MET3p::ARO4 cells of *C. albicans* (one wild-type copy of ARO4 placed under control of the repressible MET3 promoter) and found that they fail to grow in the absence of aromatic amino acids when ARO4 expression is repressed, and that this growth defect can be partially rescued by aromatic amino acids and certain aromatic amino acid pathway intermediates. It is concluded that, like *S. cerevisiae*, *C. albicans* contains two DAHP synthases required for the first step in the aromatic amino acid biosynthetic pathway.